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OF DERMATOPHYTES

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HEITI PALDROK

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ON THE VARIABILITY AND CLASSIFICATION OF DERMATOPHYTES

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HEITI PALDROK

FROM THE DEPARTMENT OF DERMATOLOGY, KAROLINSKA INSTITUTET, STOCKHOLM,
THE INSTITUTE OF SYSTEMATIC BOTANY, UNIVERSITY OF UPSALA, AND THE
INSTITUTE OF PHYSIOLOGIC BOTANY UNIVERSITY OF UPSALA, UPSALA

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1. Heiti Paldrok: On the Variability and Classification of Dermatophytes. Acta Dermat.-Venereol. 33, 1, 1953.
2. Heiti Paldrok: The Effect of Temperature on the Growth and Development of Dermatophytes. Acta Dermat.-Venereol. 35, 1, 1955.

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HÅKAN OHLSSONS BOKTRYCKERI

Introduction

Dermatophytes are the most frequently encountered among fungi parasitizing on man as well as on various mammals and birds. They produce predominantly superficial lesions which affect the skin and its appendages, hair, nails or feathers. From mucous membranes or inner organs they are isolated only exceptionally.

Botanically the dermatophytes constitute a group of closely related types within the *Hyphomycetes* of the *Fungi imperfecti*. No perfect fructifications are known with certainty, only asexual conidia.

In its pathogenic state the mycelium gives rise to smaller, regularly shaped, or larger, often irregularly roundish, more or less thick-walled spore-like bodies, which have been assumed to be "chlamydospores" (resting spores).

In cultures the dermatophytes form up to three different kinds of spores, viz., (1) small unicellular, roundish to oblong "microconidia", situated in clusters ("en grappe") or along the hyphae, (2) large multicellular "macroconidia", supported by stalks, and finally, (3) rather large, more or less thick-walled terminal or intercalary "chlamydospores". In addition to the conidia there are also structures such as spiral hyphae, "nodular bodies" and "antler-like organs". If the mycelium is irregular, swellings may occur near the crosswalls ("raquet mycelium") or they may be terminal ("terminal clubs"). If the terminal swellings occur in branched mycelium, the whole structure is called "favic chandelier". Hyphae, bearing short, denticulate projections along one side only, are called "pectinate organs".

If abundant, the spores as well as the additional structures give a powdery appearance to the cultures, in contrast to the velvety to cottony or downy appearance of cultures, in which they are scarce or absent. In a third type of cultures the aerial hyphae may be completely lacking, although in the remaining mycelium swellings and chlamydospores may be present in abundance. Such cultures have a glabrous surface and are termed "faviform".

Because of the profusion of cultural forms observed in the course of time, about 200 different species and varieties of dermatophytes have been described, and more than 25 different genera have been proposed to accommodate all the species. Yet the great number of classifications available to-day indicate, however, that an ideal system, satisfying both the botanical and clinical requirements has not yet been established.

The most appropriate was, in our opinion, that of Conant¹ based on the botanical principles laid down by Emmons.² According to the shape of their multicellular macroconidia the fungi were grouped into three genera: *Tricho-*

¹ Manual of Clinical Mycology. W. B. Saunders Company, Philadelphia and London, 1944.

² Arch. Dermat. & Syph. 30, 337, 1934.

phyton (11 species), *Microsporum* (3 species), and *Epidermophyton* (1 species). To other micromorphologic structures such as microconidia, spiral-hyphae, nodular bodies, etc., less significance was ascribed in generic diagnostics. This Emmons-Conant classification implied a decided improvement but was still not an ideal one. It did not allow for strains not conforming to the description of the different species. Moreover, cultures which fitted well into the scheme might spontaneously change into intermediate types, or even adopt characters of quite another species.

The present investigation was undertaken in the hope of arriving at a better understanding of the relations between the different types, and of the intermediate and difficultly determined strains of the dermatophytes, but also of finding correlations between the various fungous types and the clinical manifestations caused by them.

Personal Observations

The study was carried out in two sections. The first searched for new trends for the systematisation and led to a new classification based on the hypothesis that many different types of dermatophytes are only different developmental states of one and the same fungus. The second section showed that the different developmental states in dermatophytes can be induced intentionally through the influence of temperature.

I. On the Variability and Classification of Dermatophytes

The literature on the occurrence of atypical cultures and transformations of dermatophytes is reviewed. My own results are based on studies performed during a five-year period, 1946—1951, at the Department of Dermatology of the Karolinska Institutet in Stockholm, of dermatophyton-cultures, obtained from 283 cases of mycoses of predominantly Swedish origin.

To ensure uniform growth-conditions only one medium was used, the modified Sabouraud's agar with 6 per cent glucose and 1 per cent peptone. Cultivation was carried out at 25° C.

Of the total number of 292 strains, 37 were of an intermediate character. In 9 cases two different types were isolated simultaneously from the same patient. Of spontaneous variations, *Trichophyton mentagrophytes* developed both crateriform and cerebriform cultures; one *T. rubrum* was transformed into *T. epilans*; one *T. epilans*, one *Microsporum gypseum*, and two *Epidermophyton floccosum* strains were transformed into *T. rubrum*; two strains of *E. floccosum* became faviform. One of the latter at the same time showed parallel changes tending towards powdery *Trichophyton*. In addition one faviform culture in consecutive transfers assumed partly the appearance of a transitional form from *T. mentagrophytes* to *T. rubrum*, partly that of a type sometimes resembling *T. epilans* and sometimes *T. sulfureum*. In a *M. gypseum* strain two types of faviform alterations induced by fungicides were observed. On one occasion, *T. Schoenleini* changed into a type *faviforme album* following a transfer from man to man.

In the non-pathogenic state, the alterations usually occurred in aged cultures,

especially after successive transfers. They occurred in sectors or excentrically localized circular areas.

The usual mode of alterations is that cultures of a more complete morphology become poor in micromorphological structures such as macroconidia, microconidia, spiral hyphae, nodular organs, and antler-like bodies, or lose them completely. During this process the micromorphological structures simultaneously undergo a retrogression. The macroconidia of the types *trichophyton* or *microsporum* may become swollen and roundish, or slightly elongated to clavate, acquiring the shape of *epidermophyton* type. Or they may become longer and slenderer, cylindrical as the macroconidia of the *rubrum* type, and even take the form of coarser hyphae. In the latter case finally they cannot be distinguished from the surrounding mycelium. Also the microconidia which primarily are roundish, become during retrogression longer and slenderer.

The slender macroconidia of the *rubrum* type, and the elongate slender microconidia are the last of the structures to disappear in cultures with aerial mycelium.

Of the other micromorphological structures, the primary regular and tightly-coiled corkscrew-like spirals turn into irregular loosely wound structures, resembling broken spiral springs. Further they may become undulating hyphae, which in turn, becoming gradually straighter, may finally fuse like common hyphae with the surrounding mycelium. Also the remaining structures already mentioned, such as the nodular bodies and antler-like structures, may by further retrogression become filamentous.

With the loss of micromorphological structures the surface of the cultures changes from powdery into velvety, cottony or woolly (lanose). The latter alteration in dermatophyton cultures is known as "pleomorphism".

Most cultures that have turned cottony will remain so. Still the cottony stage may be followed by a further retrogression, a complete disappearing of the aerial mycelium, the cultures becoming glabrous (or faviform). However, a "faviform degeneration" need not necessarily pass the cottony stage; it may directly follow the morphologically higher developed one.

The cultures may be transformed also in the opposite direction, faviform and cottony ones changing into higher developed types.

All species or species-types of the dermatophytes have been seen to undergo some form of the alterations.

The morphological structures of all the dermatophytes being on principle identical, these fungi were united into one genus, for which *Microsporum* is the valid name. We accept only three species: *M. Audouini* (former *M. canis*), *M. gypseum*, and *M. tonsurans* (*Trichophyton mentagrophytes*). All other species described are considered as degenerative states of these three. Further, according to their developmental state all the dermatophytes were grouped into three somewhat overlapping main stages: (1) stage with complete morphology (*florentiform* stage), (2) stage displaying a cottony turf, consisting of hyphae, developing scanty micromorphologic structures in a regressive state, or of sterile hyphae only (*rubriform* stage), and (3) stage of glabrous or faviform cultures (*faviform* stage).

These stages readily concur with the clinical manifestations. The strains with a complete morphology (*florentiform* stage) cause the classical, distinctly circum-

scribed forms of dermatomycosis or tinea; the strains referable to the second (*rubriform* stage) cause the more chronic and eczematous lesions, and the *faviform* strains the clinical picture known on the whole as favus or tinea favosa.

We also see that the above stages readily agree with the features of the fungi in their pathogenic state as found in specimens. The fungi with the highest developed morphology correspond to the type of parasites which show symmetric slender mycelium and neatly arranged uniform chlamydospores. Both of the elements become irregular in shape in the less developed types, viz. the more irregular the poorer the morphology of the causative fungus.

For clinical diagnosis the type of the causative fungus should be determined in the primary culture, its developmental stage corresponding to the actual state of the disease. An intermediate position of the fungus in the scheme may reveal the changing nature of the disease from one stage into another.

II. *The Effect of Temperature on the Growth and Development of Dermatophytes*

The aim of the second study was to confirm the hypothesis that the different types of dermatophytes are actually only different developmental states of one and the same fungus, by intentionally inducing variations in the fungi, using for this purpose an environmental factor. As such a factor most easy to control the temperature was chosen, and the effect of it on the growth and development of dermatophytes on artificial media was studied. For the experiment ten different strains representing the most characteristic developmental states of dermatophytes were selected: *M. Audouini* var. *canis* (*M. canis*), *M. gypseum* (*M. gypseum*), *M. tonsurans* var. *mentagrophytes* (*T. mentagrophytes*), *M. Audouini* var. *Audouini* (*M. Audouini*), *M. floccosum* (*E. floccosum*), *M. tonsurans* var. *tonsurans* (*T. tonsurans*), *M. rubrum* (*T. rubrum*), *M. faviforme* var. *Schoenleini* type *album* (*T. Schoenleini* type *album*), *M. faviforme* var. *Schoenleini* (*T. Schoenleini*), *M. faviforme* var. *violaceum* (*T. violaceum*).

The cultivation was carried out at nine different temperatures: 6°, 10°, 15°, 19°, 25°, 30°, 37°, 40°, and 44° C. Two different media were employed: (1) Sabouraud's 6 per cent glucose, 1 per cent peptone, 2 per cent agar, and (2) a synthetic control medium, according to Robbins & Ma,¹ consisting of 0.15 per cent KH₂PO₄, 0.05 per cent MgSO₄ · 7H₂O, 0.2 per cent asparagine, 5 per cent glucose, 2 per cent agar with added vitamins of the B-group and trace elements.

Generally, growth was better on Sabouraud's agar. The temperature range for growth was widest in the highest developed types, becoming successively narrower in the less highly developed ones, and being narrowest in the *faviform* types. The minimum, ranging from 4°, 6° to 10°, and the optimum of about 30° for the vegetative growth of the dermatophytes correspond, on the whole, to the cardinal points of the fungi in general. However, the maximum of about 37°, 40°, or 44°, is somewhat above the usual maximum, and reaches the body temperature of mammals and birds. This gives the dermatophytes an opportunity to parasitize on animals, while their rather low optimum could be one of the reasons for their remaining predominantly superficial.

¹ Am. J. Bot. 32: 509, 1945.

The optimum for sporulation lies some degrees centrigrade below that for the vegetative growth. At the sporulation optimum the conidia are of normal shape, and also the other micromorphological structures are most characteristic at this temperature. The gross appearance of the cultures is most typical too at and somewhat below the optimum temperature for sporulation.

Further from the optimum the morphology is poorer with the micromorphological structures simultaneously turning retrogressive. The changes are most conspicuous in the highest developed types. The macroconidia originally of the type "*trichophyton*" or "*microsporum*" may take the shape of those of "*epidermophyton*", "*rubrum*", or "*keratomyces*". The roundish to pyriform microconidia situated in clusters become elongated and slender, and situated predominantly along the hyphae. The remaining structures, such as spirals, nodular bodies, or antler-like organs become irregular in shape, gradually less wound or less crooked, and finally fuse with the surrounding mycelium, a fate which is also encountered by macroconidia which during their retrogression have become too slender.

The formerly powdery surface of the cultures in connection with the retrogression of the micromorphological structures turns velvety or lanose, the cultures then displaying the characteristics of either the "mitigated" or human pathogen forms, an "*epidermophyton*", or a "*rubriform*" type. Still closer to the very temperature limits of growth the cultures lose their aerial part of the mycelium, getting glabrous, and simultaneously the cultures become heaped and wrinkled. Microscopically the remaining mycelium is coarse and irregular in shape, showing all formations occurring in *faviform* cultures. Thus, at the borderline of growth the fungi take the appearance of a *faviform* type.

The above-mentioned changes are reversible.

These observations support our hypothesis that the less highly developed types of the dermatophytes are actually only degenerative states of the higher developed ones.

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